REMARKS

Claims 40-44 and 51-68 are under examination in this application. All of the claims stand rejected under 35 U.S.C. § 112, second paragraph; claims 41, 43, and 44 also stand rejected under 35 U.S.C. § 112, first paragraph. These rejections are addressed below.

Drawings

As requested, Applicants agree to submit a set of formal drawings identical to those submitted on March 7, 2002. These drawings will be hand-delivered to the Examiner.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 40-44 and 51-68 stand rejected, under 35 U.S.C. § 112, second paragraph, for indefiniteness.

As an initial matter, Applicants note that the Office withdrew the indefiniteness rejection as applied to the term "randomized" in claims 40 and 42, because these claims pertain to a library of proteins. However, subsequently, the Office stated that this rejection was maintained as to what sequences are considered "randomized" in claims 40-44 and 51-68. Applicants assume that the inclusion of claims 40 and 42 in this rejection is inadvertent, since the Office withdrew this rejection on page 2 of the Office action.

Nonetheless, the arguments presented below apply with equal force to all of claims 40-44 and 51-68.

The rejection as currently applied is based on the assertion that the "claims are unclear as to what sequences are considered randomized since the claims do not contain a template sequence with which to compare." In support of this position, the Office states that (Office Action, pages 4-5):

> Many proteins contain fibronectin type III domains and the amino acid sequences of these domains vary even within one species....It is noted that [specification that] the amendment specifying that the fibronectin type III domain is "human" does not overcome the rejection because the human fibronectin type III domain also may have many different sequences (see Main et al. Cell, Vol. 71, pp. 671-676 IDS of Paper No. 3), at Figure 3, page 674).

This rejection is respectfully traversed.

Independent claims 40, 41, and 59 are reproduced below (emphasis added):

> 40. (Twice Amended) A method for obtaining a scaffold-based protein that binds to a compound, said method comprising:
> (a) contacting a compound with a library of scaffold-based proteins under conditions that allow binding to form a compound-scaffold-based protein complex, wherein the scaffold is derived from the *tenth module of human fibronectin type III (^{10}Fn3)*, said library comprising scaffold-based proteins having at least three randomized loops and being characterized by their ability to bind to a compound that is not bound by said human ^{10}Fn3; and
> (b) obtaining, from said complex, a scaffold-based protein that binds to said compound and that has at least one amino acid alteration in each of three loops relative to the human ^{10}Fn3 sequence.
>
> 41. (Twice Amended) A method for obtaining a compound that binds to a scaffold-based protein, said method comprising:
> (a) contacting a scaffold-based protein with a candidate compound under conditions that allow binding to form a compound-scaffold-based protein complex,

wherein the scaffold is derived from the *tenth module of human fibronectin type III (^{10}Fn3)*, said scaffold-based protein having at least one amino acid alteration in each of three loops relative to the human ^{10}Fn3 sequence, said scaffold-based protein being characterized by its ability to bind to a compound that is not bound by said human ^{10}Fn3; and

(b) obtaining, from said complex, a compound that binds to said scaffold-based protein.

59. (Twice Amended) A method for detecting a compound in a sample, said method comprising:

(a) contacting said sample with a scaffold-based protein which binds to said compound under conditions that allow binding to form a compound-scaffold-based protein complex, wherein the scaffold is derived from the *tenth module of human fibronectin type III (^{10}Fn3)*, said scaffold-based protein having at least one amino acid alteration in each of three loops relative to the human ^{10}Fn3 sequence, said scaffold-based protein being characterized by its ability to bind to a compound that is not bound by said human ^{10}Fn3; and

(b) detecting said complex, thereby detecting said compound in said sample.

As indicated, in each of these claims, the template sequence against which a randomized protein is compared is clearly specified to be "the tenth module of human fibronectin type III (^{10}Fn3)." The indefiniteness rejection is traversed because this ^{10}Fn3 template has only one sequence. The Office's assertion that "many proteins contain fibronectin type III domains" is correct, but it ignores the limitation in the claims that the invention pertains only to the *tenth module* of human fibronectin type III, and there has been no showing that there is more than one tenth module of human fibronectin type III.

The Office also relies for support of this rejection on Figure 3 of Main et al., Cell 71: 671-678 and the assertion that "the human fibronectin type III domain also may have many different sequences." This assertion is incorrect and is based on a misinterpretation

of Main Figure 3. This Figure does not indicate that there are multiple sequences for the tenth module of human fibronectin type III, but rather shows that there are sixteen known modules of type III fibronectin that make up this protein (i.e., "F1"-"F16"), all of which share some degree of relatedness. These sequences therefore do not represent many different sequences for the tenth module of human fibronectin type III protein, but instead represent the one tenth module and the various other fibronectin type II modules that make up the protein. Consistent with Applicants' position, this Figure lists only one amino acid sequence for Applicants' claimed tenth module (i.e., "F10"), illustrating that for the tenth module of the human fibronectin type III protein, one sequence, rather than many sequences, exists.[1] Thus, this basis for the § 112 rejection may be withdrawn.

Claim 59 remains rejected as indefinite based on the assertion that the term "randomized" cannot properly refer to a single protein. The Office is again directed to Applicants' specification at page 9, lines 1-2, where the term "randomized" is explicitly defined:

> By "randomized" is meant including one or more amino acid alterations relative to a template sequence.

Applicants have now amended claim 59 to replace the term randomized with language from its definition. This amendment addresses the Office's concern, in that the claim

[1] The existence of only one amino acid sequence for the tenth module of human fibronectin type III is further supported by Dickinson et al., J. Mol. Biol. 236:1079-1092 (1994) (see Figure 8 and text section (g)), previously made of record in this case.

recites that the scaffold-based protein is derived from the human ^{10}Fn3 sequence and has at least one amino acid alteration in each of three loops relative to the human ^{10}Fn3 sequence.[2] The § 112 rejection as applied to claim 59 should be withdrawn.

Claims 40, 42, 44, 51, 53-56, and 58 stand newly rejected as indefinite based on the assertion that claim 40 and its dependent claims lack essential steps. While Applicants disagree with this rejection, independent claim 40 has been amended, and this rejection may be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 41, 43, and 44 stand further rejected, under 35 U.S.C. § 112, first paragraph as lacking enablement. This rejection turns on the assertion that "the specification has not taught how to practice the claimed method wherein the number of loops that are involved in binding can be predicted or controlled" and focuses on Applicants' claim limitation "wherein the binding ability results from the randomization of said at least three loops."

Without agreeing with the Examiner, and merely to expedite prosecution, Applicants have amended claim 41 to eliminate this requirement. (Parallel amendments have also been made to claims 40 and 59). This rejection may now be withdrawn.

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[2] Parallel amendments have also been made to independent claims 40 and 41.

Information Disclosure Statement

Applicants note that the Form PTO-1449 that was submitted with an Information Disclosure Statement filed on September 6, 2001 has not been initialed and returned, and hereby request that it be initialed and returned with the next Office action.

Conclusion

Applicants submit that this case is in condition for allowance, and such action is respectfully requested.

Enclosed is a Petition to extend the period for replying to the Office action for three months, to and including December 18, 2002. The Office is authorized to charge Applicants' Deposit Account for the required extension fee.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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Version of Claims Showing Changes Made

40. (Twice Amended) A method for obtaining a scaffold-based protein that binds to a compound, said method comprising:

(a) contacting a compound with a library of scaffold-based [candidate] proteins under conditions that allow binding to form a compound-scaffold-based protein complex, wherein the scaffold is derived from the tenth module of [the] human fibronectin type III [domain] (^{10}Fn3), said library comprising scaffold-based proteins having at least [one] three randomized loops and being [said library comprising scaffold-based proteins] characterized by their ability to bind to a compound[s] that [are] is not bound by said human ^{10}Fn3 [fibronectin type III domain and wherein said binding ability results from the randomization of at least one loop, said contacting being carried out under conditions that allow binding to form a compound-scaffold-based protein complex]; and

(b) obtaining, from said complex, a scaffold-based protein [having at least three randomized loops] that binds to said compound and that has at least one amino acid alteration in each of three loops relative to the human ^{10}Fn3 sequence.

41. (Twice Amended) A method for obtaining a compound that binds to a scaffold-based protein, said method comprising:

(a) contacting a scaffold-based protein with a candidate compound under

conditions that allow binding to form a compound-scaffold-based protein complex, wherein the scaffold is derived from the tenth module of [the] human fibronectin type III [domain] (^{10}Fn3), said scaffold-based protein having at least one amino acid alteration in each of three loops relative to the human ^{10}Fn3 sequence [three randomized loops], said scaffold-based protein being characterized by its ability to bind to a compound that is not bound by said human ^{10}Fn3 [fibronectin type III domain and wherein the binding ability results from the randomization of said at least three loops, said contacting being carried out under conditions that allow binding to form a compound-scaffold-based protein complex]; and

(b) obtaining, from said complex, a compound that binds to said scaffold-based protein.

59. (Amended) A method for detecting a compound in a sample, said method comprising:

(a) contacting said sample with a scaffold-based protein which binds to said compound under conditions that allow binding to form a compound-scaffold-based protein complex, wherein the scaffold is derived from the tenth module of [the] human fibronectin type III [domain] (^{10}Fn3), said scaffold-based protein having at least one amino acid alteration in each of three loops relative to the human ^{10}Fn3 sequence [three randomized loops], said scaffold-based protein being characterized by its ability to bind to

a compound that is not bound by said human ^{10}Fn3 [fibronectin type III domain and wherein the binding ability results from the randomization of said at least three loops, said contacting being carried out under conditions that allow binding to form a compound-scaffold-based protein complex]; and

(b) detecting said complex, thereby detecting said compound in said sample.

U.S. Serial No. 09/515,260

Claims Pending After Entry of Amendment

40. (Twice Amended) A method for obtaining a scaffold-based protein that binds to a compound, said method comprising:

(a) contacting a compound with a library of scaffold-based proteins under conditions that allow binding to form a compound-scaffold-based protein complex, wherein the scaffold is derived from the tenth module of human fibronectin type III (^{10}Fn3), said library comprising scaffold-based proteins having at least three randomized loops and being characterized by their ability to bind to a compound that is not bound by said human ^{10}Fn3; and

(b) obtaining, from said complex, a scaffold-based protein that binds to said compound and that has at least one amino acid alteration in each of three loops relative to the human ^{10}Fn3 sequence.

41. (Twice Amended) A method for obtaining a compound that binds to a scaffold-based protein, said method comprising:

(a) contacting a scaffold-based protein with a candidate compound under conditions that allow binding to form a compound-scaffold-based protein complex, wherein the scaffold is derived from the tenth module of human fibronectin type III

(^{10}Fn3), said scaffold-based protein having at least one amino acid alteration in each of three loops relative to the human ^{10}Fn3 sequence, said scaffold-based protein being characterized by its ability to bind to a compound that is not bound by said human ^{10}Fn3; and

(b) obtaining, from said complex, a compound that binds to said scaffold-based protein.

42. (Amended) The method of claim 40, said method further comprising further randomizing at least one loop of said human fibronectin type III domain of said protein obtained in step (b) and repeating said steps (a) and (b) using said further randomized protein.

43. The method of claim 41, said method further comprising modifying said compound obtained in step (b) and repeating said steps (a) and (b) using said further modified compound.

44. The method of claim 40 or 41, wherein said compound is a protein.

51. (Amended) The method of claim 40 or 41, wherein at least one of said randomized loops is extended in length relative to the corresponding loop of human

^{10}Fn3.

52. (Amended) The method of claim 40 or 41, wherein said ^{10}Fn3 lacks an integrin-binding motif.

53. The method of claim 40 or 41, wherein said protein is covalently bound to a nucleic acid.

54. The method of claim 53, wherein said nucleic acid encodes said protein.

55. The method of claim 53, wherein said nucleic acid is RNA.

56. The method of claim 40, wherein said compound is immobilized on a solid support.

57. (Amended) The method of claim 41, wherein said scaffold-based protein is immobilized on a solid support.

58. The method of claim 56 or 57, wherein said solid support is a column or microchip.

59. (Twice Amended) A method for detecting a compound in a sample, said method comprising:

(a) contacting said sample with a scaffold-based protein which binds to said compound under conditions that allow binding to form a compound-scaffold-based protein complex, wherein the scaffold is derived from the tenth module of human fibronectin type III (^{10}Fn3), said scaffold-based protein having at least one amino acid alteration in each of three loops relative to the human ^{10}Fn3 sequence, said scaffold-based protein being characterized by its ability to bind to a compound that is not bound by said human ^{10}Fn3; and

(b) detecting said complex, thereby detecting said compound in said sample.

60. (Amended) The method of claim 59, wherein said scaffold-based protein is immobilized on a solid support.

61. (Amended) The method of claim 60, wherein said scaffold-based protein is immobilized on said solid support as part of an array.

62. The method of claim 60, wherein said solid support is a chip or bead.

63. (Amended) The method of claim 59, wherein said scaffold-based protein is

covalently bound to a nucleic acid.

64. (Amended) The method of claim 63, wherein said nucleic acid encodes said scaffold-based protein.

65. The method of claim 64, wherein said nucleic acid is RNA.

66. The method of claim 59, wherein said compound is a protein.

67. The method of claim 59, wherein said compound is detected by radiography, fluorescence detection, mass spectroscopy, or surface plasmon resonance.

68. (New) The method of claim 40, wherein the proteins of said library have at least three randomized loops.